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ORIGINAL ARTICLE

Impact of Active *Helicobacter pylori* Infection on Disability and Relapses in Multiple Sclerosis

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Abstract

Background: Multiple sclerosis (MS) is a chronic, inflammatory, and demyelinating disorder of the central nervous system, affecting primarily adults. The disease involves the immune system that damages the myelin sheath of neurons, but its exact cause remains unclear. Multiple sclerosis is believed to be multifactorial, with genetic, environmental, infectious, and noninfectious factors, including vitamin D deficiency, low sun exposure, obesity in childhood or adolescence, and smoking, associated with increased risk.
Objective: To evaluate the relationship between an active *Helicobacter pylori* infection and the progression of MS, particularly its effect on the rate of relapse and the progression of disability associated with the disease.
Methods: A cross-sectional study was conducted at the Kirkuk MS Clinic at Azadi Teaching Hospital. The study included 100 patients diagnosed with MS according to the McDonald criteria, who were divided into two groups: MS with positive and negative *H. pylori*. The collected clinical data included demographic characteristics, disease duration, relapse history, and disability scores.
Results: A significant difference in relapse and disability EDSS scores ($P = 0.001$ and $P < 0.001$, respectively) was observed; however, no significant differences were observed in sex, age, or disease duration between the two groups.
Conclusion: *H. pylori* infection may lead to more severe and disabling forms of MS, suggesting the importance of screening for and management of MS patients.

1. Introduction

Multiple Sclerosis (MS) is a neurological disorder that affects many young people and is characterized by demyelination, neurodegeneration, and varying degrees of neurological disability. It primarily affects young adults, especially women, and follows a relapsing or progressive course [1]. The pathogenesis of MS is complex and not yet fully understood. However, it is generally considered a multifactorial disease influenced by genetic predisposition, environmental exposures, and infectious or noninfectious triggers [2]. Among the infectious agents implicated, *Helicobacter pylori* has received increasing attention in recent years [3,4].

H. pylori is a Gram-negative microaerophilic bacterium that colonizes the human stomach and is widely known for its role in gastritis, peptic ulcers, and gastric cancer. However, emerging evidence suggests that its impact extends beyond the gastrointestinal tract and can influence autoimmune and neurological diseases [5,6]. The relationship between

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H. pylori infection and autoimmune diseases such as MS has sparked a continuous debate. Some studies have reported that chronic *H. pylori* infection may exert a protective and immune-modulating effect against MS by inducing regulatory T cell responses and promoting immune tolerance. For instance, several epidemiological investigations and meta-analyses have suggested a lower prevalence of *H. pylori* infection among MS patients compared to healthy controls, implying a possible protective role [7,8].

However, other studies have highlighted the possibility that active *H. pylori* infection, particularly in genetically predisposed individuals, may exacerbate autoimmune activity and worsen disease outcomes. Recent findings have demonstrated that *H. pylori* can induce systemic inflammation and alter cytokine profiles, which could contribute to increased MS disease activity. Notably, some reports indicate that active *H. pylori* infection is associated with higher relapse rates and more severe neurological impairment [9,10]. However, this remains controversial and not fully validated in different populations.

The conflicting nature of these findings highlights a critical gap in our understanding of the true impact of *H. pylori* on the clinical course of MS. Although the presence of *H. pylori* may attenuate or exacerbate disease progression, depending on host and bacterial factors, the exact role of active infection, particularly as assessed by direct diagnostic tools such as stool antigen testing, remains poorly studied.

The present study aims to investigate the relationship between active *H. pylori* infection and MS activity, as measured by relapse frequency and disability scores (EDSS). By comparing MS patients with and without active *H. pylori* infection using a monoclonal ELISA-based stool antigen test, this study aims to provide clearer evidence on whether *H. pylori* contributes to a more active and disabling disease course. Clarifying this relationship may have implications for both prognostic evaluation and the development of adjunctive management strategies in MS.

2. Materials and Methods

This cross-sectional study was conducted at the Multiple Sclerosis (MS) Clinic at Azadi Teaching Hospital in Kirkuk City, Iraq, from January 2024 to January 2025. A total of 100 patients diagnosed with relapsing-remitting multiple sclerosis (RRMS) were enrolled based on the 2017 McDonald criteria. Participants were divided into two groups based on their *H. pylori* status: MS patients with and without active *H. pylori* infection. The inclusion criteria for MS patients were as follows: age between 18 and 55 years, disease duration of at least 1 year, stable treatment with disease-modifying therapy, and no use of antibiotics or proton pump inhibitors within 2 weeks before testing.

On the other hand, the exclusion criteria were prior *H. pylori* eradication therapy, recent infections or immunosuppressive therapy, comorbid autoimmune, gastrointestinal, or systemic diseases, and pregnancy or breastfeeding.

Active *H. pylori* infection was determined using Premier Platinum HpSA Plus monoclonal stool antigen ELISA (Meridian Bioscience, USA). Participants were asked to provide fresh stool samples. A positive test indicated an active *H. pylori* infection.

All MS patients were examined neurologically by a consultant neurologist. The evaluation included measurement of the Expanded Disability Status Scale (EDSS) at enrollment to determine the level of neurological disability, with documentation of relapse numbers in previous years. In addition, demographic data, clinical history, disease duration, and *H. pylori* infection status were systematically recorded.

2.1. Statistical analysis

Data were entered and analyzed using JASP software version 0.19.3. Descriptive statistics were used to summarize participant characteristics, and analyses of continuous variables were performed by using Student's t-test, presented as mean ± standard deviation (SD). The Chi-square test compared categorical variables. Multivariate regression analysis was performed to explore the association between *H. pylori* status and both EDSS scores and relapses, adjusting for confounding variables such as age, sex, and disease duration. A P-value < 0.05 was considered statistically significant.

The approval protocol was provided by the Research Ethics Committee of the College of Medicine, University of Kirkuk (Document no. 69, dated 14-5-2025). All participants provided written informed consent. All procedures adhered to the ethical principles outlined in the Declaration of Helsinki.

3. Results

A total of 100 patients with MS were included in the study and classified based on their *H. pylori* infection status into two groups: the *H. pylori*-positive and the *H. pylori*-negative. The demographic and clinical characteristics were compared between these two groups. Age distribution and sex were comparable, with no statistically significant differences observed (P = 0.220 and P = 0.870, respectively). The mean duration of disease was also similar between the two groups, with an average of 4.73 ± 1.59 years in the positive group for *H. pylori* and 4.57 ± 1.61 years in the *H. pylori*-negative group (P = 0.629).

The differences were significant in clinical outcomes. Patients with positive tests for H. *pylori* had a noticeably more frequent relapse (mean 0.90 ± 0.96) compared to the *H. pylori*-negative group (mean 0.38 ± 0.61), with a P-value of 0.001. Similarly, the EDSS scores, which reflect the degree of neurological disability, were significantly elevated in the *H. pylori*-positive group (4.18 ± 1.57) versus the negative group (2.57 ± 0.89), with a P-value of < 0.001 **(**Table 1**)**.

To further explore the association between *H. pylori* status and both EDSS score and relapses, a multivariate

Table (1): Demographic characteristics of the studied group.

Variables	MS +ve *H. pylori*	MS -ve *H. pylori*	*P*
Age groups (years) No. (%)			
<25	3 (3)	2 (2)	0.220*
26–35	23 (23)	27 (27)	
>36	14 (14)	31 (31)	
Sex No. (%)			
Male	20 (20)	31 (31)	0.870*
Female	20 (20)	29 (29)	
Disease duration (years) (Mean ± SD)	4.725 ± 1.585	4.567 ± 1.609	0.629**
Relapses (relapse/year) (Mean ± SD)	0.900 ± 0.955	0.383± 0.613	**0.001****
EDSS score (Mean ± SD)	4.175 ± 1.567	2.567 ± 0.890	**<0.001****

*Chi square; **Student's t-test; EDSS = Expanded Disability Status Scale; *H. pylori* = *Helicobacter pylori*; MS = Multiple sclerosis; SD = Standard deviation; +ve = Positive; −ve = Negative.

regression analysis was performed, adjusting for potential confounding variables including age, sex, and disease duration. The analysis demonstrated a statistically significant overall multivariate effect of *H. pylori* status on the combined dependent variables (Wilks' Lambda = 0.638, F (2, 94) = 26.61, $P < 0.001$). In the individual regression models, H. pylori negative status was associated with a significant reduction in EDSS scores (B = –1.65, $P < 0.001$) and relapse rates (B = –0.50, $P < 0.001$). These associations remained significant after adjusting for confounders. Notably, disease duration was also independently associated with an increased relapse (B = +0.29, $P < 0.001$), while age and sex were not significantly associated with either outcome (Figure 1).

4. Discussion

Multiple sclerosis is an autoimmune condition of the neurological system defined by chronic inflammation, demyelination, and progressive neurological dysfunction [11]. The disease is thought to arise from a combination of genetic susceptibility and environmental triggers, including infectious agents. Among the pathogens proposed to play a role in the pathogenesis or progression of MS [12] is a bacterium that typically colonizes the gastric mucosa, known as *H. pylori*, which is well known for its role in peptic ulcer disease and gastric malignancy [13,14]. However, over the past decade, its potential influence on autoimmune and neurological disorders has attracted considerable interest.

The association between *H. pylori* and MS is particularly complex and remains a subject of debate. One of the most challenging aspects of this association is the apparent dual nature of the effects of *H. pylori*. The study by Kountouras et al. suggests that it may exert a protective effect or could worsen MS disease outcomes [15]. This divergence likely stems from differences in study populations, definitions of infection (e.g., past exposure versus active infection), and methodologies used for detecting *H. pylori*.

In the current study, we specifically evaluated the impact of active *H. pylori* infection, determined by a monoclonal ELISA-based stool antigen test, on relapse rates and disability scores (EDSS) among 100 patients with MS. Our findings revealed that patients with active *H. pylori* infection had significantly higher relapses and more severe disability scores compared to those without the infection. These associations remained statistically significant even after adjusting for age, sex, and disease duration through multivariate regression analysis. These results suggest that active *H. pylori* may be related to a more aggressive clinical course in MS.

Our findings align with several recent studies that have reported similar associations. For instance, studies found that MS has an infectious origin with *H. pylori*, attributing this effect to elevated levels of proinflammatory cytokines and immune dysregulation induced by the bacterium [16,17]. Likewise, Zhang et al. suggested that chronic infection with *H. pylori* might aggravate MS symptoms due to systemic immune activation [18]. These studies support the idea that active bacterial infection may intensify autoimmune responses in MS patients through mechanisms such as molecular mimicry and immune cross-reactivity.

However, our results contrast with other studies that propose a protective role of *H. pylori* in MS. Our study results reported a reduced prevalence of *H. pylori* infection in MS participants compared to controls, indicating a possible immunomodulatory benefit. They hypothesized that early life exposure to *H. pylori* could promote immune tolerance and decrease the risk of autoimmune diseases, including MS [19]. One major difference that may explain this discrepancy is the method used to detect infection. While those studies assessed past exposure using serological tests for *H. pylori* antibodies, our study focused specifically on active infection, which may have different immunological consequences. Antibody presence does not necessarily indicate ongoing bacterial activity [20], whereas stool antigen testing reflects current colonization and immune interaction [21].

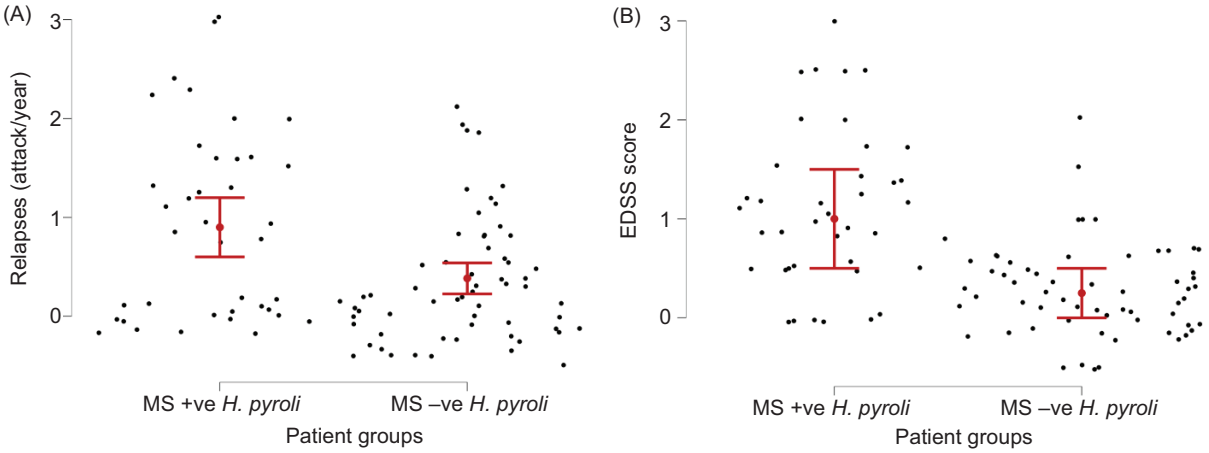

Figure (1): Multivariate regression analysis; (A) The effect of *H. pylori* status on relapses. (B) The effect of *H. pylori* status on EDSS score.

Another factor that could contribute to contrasting findings is the geographic and genetic variability in host response to *H. pylori* infection [22]. Our study was conducted in Kirkuk, Iraq, where environmental exposures, strain variations of *H. pylori*, and genetic predispositions may differ significantly from populations in Europe or North America. Furthermore, differences in healthcare access, nutritional status, and treatment adherence may influence both infection patterns and MS outcomes.

Despite the important insights gained, our research has many limitations. First, a causal relationship between *H. pylori* infection and MS activity was precluded by the cross-sectional study design. Longitudinal studies are needed to assess whether eradication of the bacterium leads to improved clinical outcomes. Second, although we used a sensitive and specific method for detecting active infection, we did not evaluate strain-specific virulence factors (e.g., CagA or VacA status), which may modulate the immunological impact of *H. pylori*. Third, while we controlled for some potential confounders, residual confounding by unmeasured factors such as diet, vitamin D levels, or socioeconomic status cannot be excluded. Lastly, the sample size, although adequate for detecting significant differences, limits generalizability, and larger multicenter studies would be beneficial to validate these findings across broader samples.

In conclusion, our study suggests that active *H. pylori* infection may negatively affect the clinical course of MS, contributing to increased relapses and greater neurological disability. These findings underscore the need for further investigation into the role of infectious agents in MS progression and raise the possibility of identifying and treating active infections that may become part of a broader, more personalized approach to MS management.

5. Conclusion

H. pylori status exhibited significantly higher relapses and greater disability as measured by EDSS scores, which indicated that *H. pylori* infection may be associated with a more active and disabling form of MS, highlighting the potential importance of screening for and addressing this infection in the therapeutic approach of MS patients.

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Authors Contributions

S.A.T: Laboratory investigations, methodology. I.N.M: Laboratory investigations, data analysis, writing. M.A.T: Collection of cases, supervision, validation, and resources. E.A.M: Conceptualization, formal analysis, writing, review & editing.

Conflicts of Interest

There are no conflicts of interest.

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